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| 10/687,402 | 10/16/2003 | Jaya Sivaswami Tyagi | AP35478 066123.0125 | 8618 |
| 21003 | 7590 | 05/30/2008 | EXAMINER | |
| BAKER BOTTS LLP. | | | FERNANDEZ, SUSAN EMILY | |
| 30 ROCKEFELLER PLAZA | | | ART UNIT | PAPER NUMBER |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| | | |
|------------------------------|---------------------------------------|-------------------------------------|
| Office Action Summary | Application No. 10/687,402 | Applicant(s) TYAGI ET AL. |
| | Examiner SUSAN E. FERNANDEZ | Art Unit 1651 |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 25 February 2008.

2a) This action is FINAL. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 38-52 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 38-52 is/are rejected.

7) Claim(s) 38-52 is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) Notice of References Cited (PTO-892)
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
 3) Information Disclosure Statement(s) (PTO/DS/06)
 Paper No(s)/Mail Date _____

4) Interview Summary (PTO-413)
 Paper No(s)/Mail Date. _____

5) Notice of Informal Patent Application
 6) Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 25, 2008 has been entered.

Claims 1-37 are canceled. Claims 38-52 are new.

Election/Restrictions

As pointed out in the office action filed December 27, 2004, the applicant's election with traverse of Group I, drawn to a screening method for inhibitors of pathogenic microbes having DevR-DevS and/or DevR-Rv2027c and its homologues, and the species wherein DevS₅₇₈ is the DevS derivative, Rv2027₁₉₄ is the Rv2027 derivative, and DevRN₁₄₅ is the DevR derivative, in the reply filed December 9, 2004, is acknowledged.

Claims 38-52 are examined on the merits to the extent they read on the elected subject matter.

Claim Objections

Claims 38-52 are objected to because of the following informalities: The first instance of "*M. tuberculosis*" should be replaced with the full name of the species, "*Mycobacterium tuberculosis*." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

First, the recitation "...the first component being a hypoxia-responsive element..." in parent claim 38 is considered new matter. The instant specification indicates that "The DevR-DevS...two-component system has been suggested to play a regulatory role during oxygen limitation on account of its hypoxia-responsive pattern of gene expression" (page 4, paragraph [0007]) and that "It is known that this two-component system is responsive to hypoxia" (page 13, paragraph [0027]). Clearly, the specification teaches that the DevR-DevS system, rather than the first component (peptides comprising the DevS or Rv2027c domains), is hypoxia-responsive.

Additionally, parent claim 38 comprises new matter given the recitation in step c) that the relative levels of phosphorylation of the second component (catalytically active DevR domain) are determined and used to indicate that the test compound is a candidate for preventing *M. tuberculosis* from entering the dormant stage of the lifecycle. Paragraph [0064] on pages 27 and 28 of the disclosure state that the drug potential of a test compound is determined based on the "degree of phosphotransfer-based dephosphorylation of DevR and its single domain derivative."

Moreover, in reference to the assay, paragraph [0176] on page 66 speaks of the transfer of phosphoryl moiety from sensor kinase of DevR protein. Thus, with respect to screening test compounds, the disclosure speaks of the dephosphorylation of the second component, rather than its phosphorylation.

Because the specification as filed fails to provide clear support for the new claim language, a new matter rejection is clearly proper.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 47 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 47 is indefinite because it recites "...the first and second components comprise full length DevR and DevS proteins, respectively" though DevS is considered the "first component" and DevR is considered the "second component."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 38-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoch et al. (US Patent 6,043,045) in view of Dasgupta et al. (2000, *Tubercle and Lung Disease*, 80(3): 141-159) and Sherman et al. (PNAS. June 19, 2001. 98(13): 7534-7539, listed on 12/9/04 IDS).

Hoch et al. discloses a method for identifying new antibiotic, antibacterial, or antimicrobial agents by inhibition of bacterial two-component systems. Specifically, agents are sought that cause the “inhibition of either the autophosphorylation or the subsequent phosphor-transfer” (column 2, lines 16-23). Furthermore, the conventional use of SDS-PAGE to assay two-component systems is described (column 2, lines 24-35), where autoradiographic analysis is used. Hoch et al. provides a high-throughput screening assay for histidine protein kinase for agent identification (column 22, lines 16-24), as described in Example 1 starting at lines 30 of column 15. In this high-throughput screening assay, the histidine protein kinase (KinA) and its substrate (SpoOF) are expressed in *E.coli* and purified (column 15, lines 45-47). This can be considered the overexpression of the histidine protein kinase. This high-throughput screening

assay measures the extent of phosphorylation of the substrate and the radioactivity remaining on a resin (column 2, lines 50-53 and column 17, lines 43-45) following SDS-PAGE analysis.

Hoch et al. does not expressly disclose the use of their methods for screening a test compound for preventing *M. tuberculosis* from entering the dormant stage in its life cycle wherein phosphorylation of DevS or Rv2027c and DevR is determined and used for judging a test compound.

Dasgupta et al. discloses the DevR-DevS two-component system in mycobacteria, specifically *M. tuberculosis*, as well as the homology of Rv2027c with DevS. It is obvious that DevS₅₇₈, Rv2027₁₉₄, and DevRN₁₄₅ would share common characteristics with DevS, Rv2027 and DevR respectively because, as evidenced by Dasgupta (Figure 3, page 148 and Figure 5, page 150), the claimed portions each contain the catalytic site of the molecules, based on the size of the transcripts disclosed in the reference.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to apply the methods of Hoch et al. to the DevR-DevS system and the known homolog of DevR-Rv2027c system as described in Dasgupta et al. in *E. coli*. The DevR-DevS and DevR-Rv2027c systems both comprise a histidine protein kinase (DevS or Rv2027c), thus being appropriate as a target of the Hoch invention. By applying the Hoch invention to the DevR-DevS system, it would be obvious that an agent positively identified could be used against tuberculosis or other diseases caused by mycobacteria such as *M. tuberculosis*, and therefore prevent *M. tuberculosis* from entering the dormant stage of its life cycle.

One of ordinary skill in the art would have been motivated to do this because Dasgupta et al. concludes that "the devR-devS two-component system may thus serve as a novel target for

anti-tubercular therapy" (page 158, second paragraph). Tuberculosis is a critical issue, so there is a high incentive to develop or determine compounds for its treatment. There would have been a reasonable expectation of success that the Hoch invention could be used for bacteria such as *M. tuberculosis* that have DevR-DevS and/or DevR-Rv2027c and its homologues based on the fact that Hoch's assay techniques are disclosed as measuring the same reactions catalyzed by Dasgupta's tuberculosis phosphorylases. Finally, it would have been obvious to have used the changes in the levels of phosphorylation of the two components to judge test compounds given that the same is done for the histidine protein kinase systems of the Hoch reference. In sum, the system of Dasgupta et al. would appear to be just the kind of system that Hoch et al. suggests their methods are applicable for.

The references differ from the claimed invention in that they do not disclose that the first component of the two-component signaling system is a hypoxia-responsive element. However, with respect to the claimed two-component system, the instant disclosure states that "It is known that this two-component system is responsive to hypoxia" (page 13, paragraph [0027]), pointing to the Sherman et al. reference as support. See also the last paragraph on page 7538 of Sherman et al. Thus, it is recognized in the prior art that the two-component system described in the instant claims is hypoxia-responsive. Moreover, even if the prior art did not teach that the first component is a hypoxia-responsive element, it is noted that MPEP 2112, Section I indicates that "...the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable." Also, the claims do not require that the first component actively responds to hypoxia.

A holding of obviousness is therefore proper.

Response to Arguments

Applicant's arguments filed February 25, 2008, have been fully considered but they are not persuasive. Also described above, Sherman et al. provides evidence that the claimed two-component system was recognized in the prior art as hypoxia-responsive. Clearly the property of being hypoxia-responsive is inherent in the claimed two-component system. Moreover, the claims under examination do not require that any response to hypoxia takes place. Thus, the claims must be rejected over the prior art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN E. FERNANDEZ whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1651

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford Jr/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
Art Unit 1651

sef